Lesson 3
Explain

Dose-Response Relationships

At a Glance

Overview

Students complete their observations of the germinating seeds on the third consecutive day. They express their data on a graph and develop a dose-response curve for their chemical. Students then compare the data from their investigation of a chemical with those of other teams and other chemicals. Students learn to analyze dose-response curves to determine threshold and potency.

Major Concepts

Dose and response are related and can be represented by a dose-response curve. Data from toxicology testing can be represented by a dose-response curve, from which scientists can describe the threshold and potency of chemicals.

Objectives

After completing this lesson, students will

- be able to describe the response seeds have to certain doses of chemicals,
- recognize that dose and response are related and be able to represent that relationship on a graph,
- compare the threshold and potency of chemicals, and
- be able to draw conclusions based on their seed investigation that relate to chemicals in the environment.

Background Information

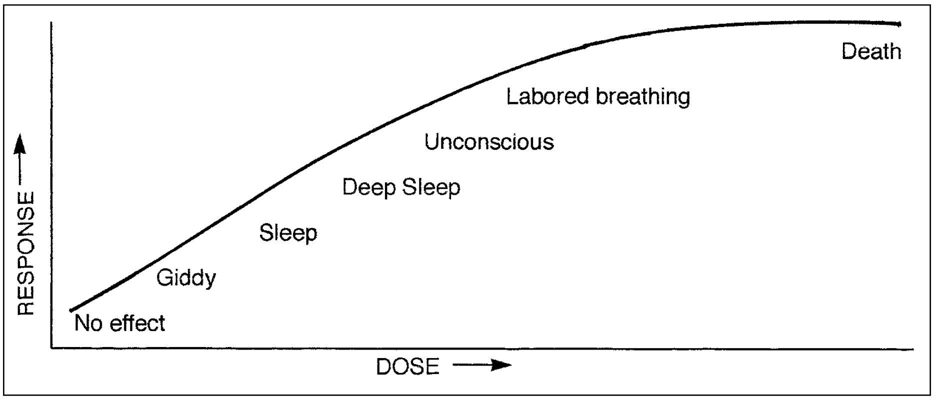
Dose-Response Curves

The characteristics of exposure to a chemical and the spectrum of effects caused by the chemical come together in a correlative relationship that toxicologists call the **dose-response relationship**. This relationship is the most fundamental and pervasive concept in toxicology.[1] To understand the potential hazard of a specific chemical, toxicologists must know both the type of effect it produces and the amount, or dose, required to produce that effect.

The relationship of dose to response can be illustrated as a graph called a dose-response curve. There are two types of dose-response curves: one that describes the graded responses of an *individual* to varying doses of the chemical and one that describes the distribution of responses to different doses in a *population* of individuals. The dose is represented on the *x*-axis. The response is represented on the *y*-axis.

The following graph shows a simple example of a dose-response curve for an individual with a single exposure to the chemical ethanol (alcohol), with graded responses between no effect and death.[2]

Individual Dose-Response Curve



From: Marczewski, A.E., and Kamrin, M. *Toxicology for the citizen* (Figure 6). Institute for Environmental Toxicology, Michigan State University, reprinted with permission.

A simple example of a dose-response curve for a population of mice in a study of a carcinogenic chemical might look like the following graph:

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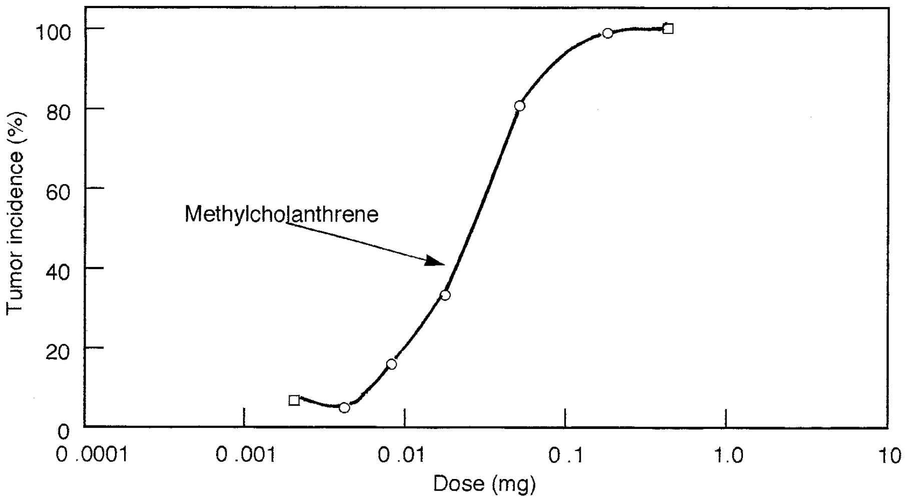
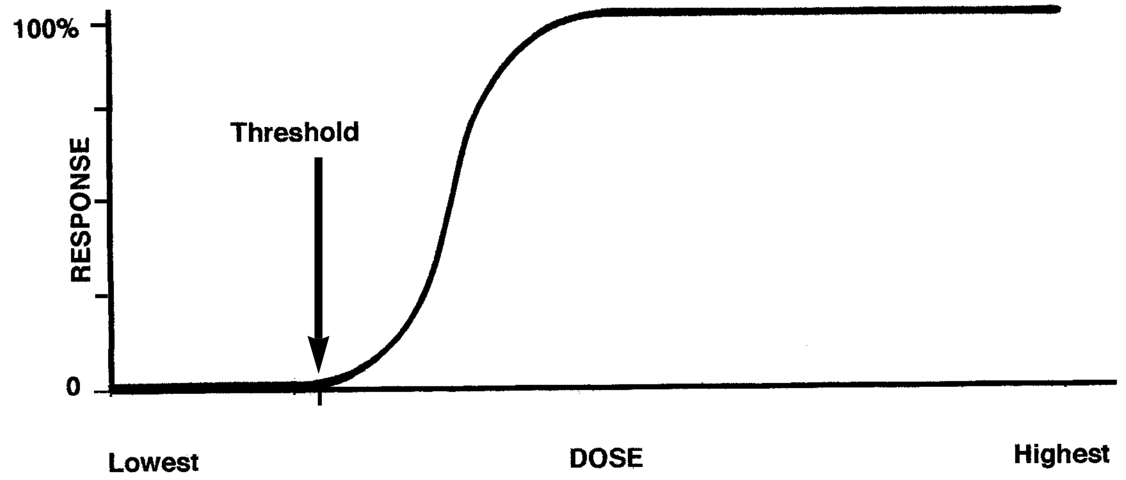


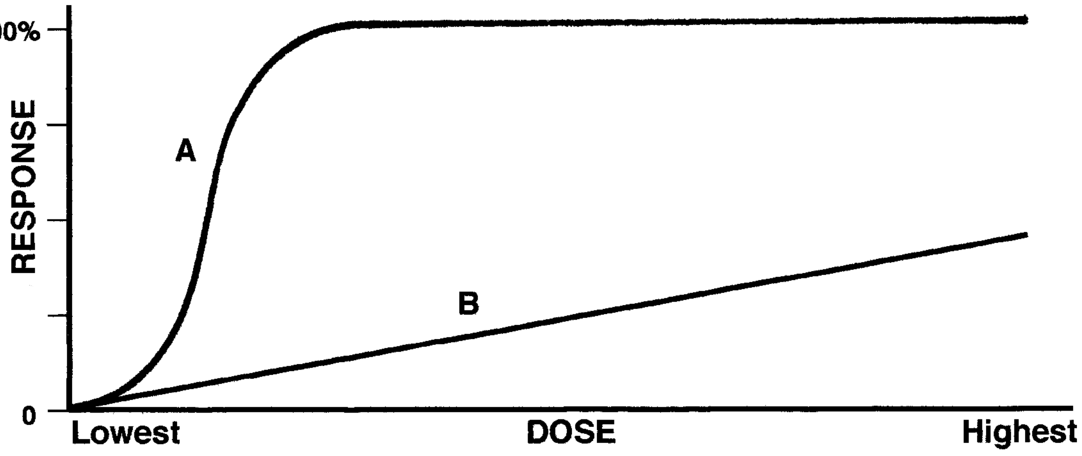
Adapted from: Eaton, D.L., and Klaassen, C.D. 1996. Principles of toxicology. In *Casarett & Doulls' toxicology: The basic science of poisons* (5th ed.). New York: McGraw-Hill.

An important aspect of dose-response relationships is the concept of **threshold**. For most types of toxic responses, there is a dose, called a threshold, below which there are no adverse effects from exposure to the chemical. The human body has defenses against many toxic agents. Cells in human organs, especially in the liver and kidneys, break down chemicals into nontoxic substances that can be eliminated from the body in urine and feces. In this way, the human body can take some toxic insult (at a dose that is below the threshold) and still remain healthy.

The identification of the threshold beyond which the human body cannot remain healthy depends on the type of response that is measured and can vary depending on the individual being tested. Thresholds based on acute responses, such as death, are more easily determined, while thresholds for chemicals that cause cancer or other chronic responses are harder to determine. Even so, it is important for toxicologists to identify a level of exposure to a chemical at which there is no effect and to determine thresholds when possible.



When a threshold is difficult to determine, toxicologists look at the slope of the dose-response curve to give them information about the toxicity of a chemical. A sharp increase in the slope of the curve can suggest increasingly higher risks of toxic responses as the dose increases, as illustrated by line A on the next graph. A relatively flat slope suggests that the effect of an increase in dose is minimal (line B).



A comparison of dose-response curves among chemicals can offer information about the chemicals as well. A steep curve that begins to climb even at a small dose suggests a chemical of high potency. The **potency** of a chemical is a measure of its strength as a poison compared with other chemicals. The more potent the chemical, the less it takes to kill.[3] In the previous dose-response graph, line A describes a chemical that is more potent than the chemical described by line B, as can be seen by the relative positions of the lines along the dosage axis and their slopes.

Although some dose-response tests use lethality as an index, toxicologists also make observations of responses that do not include death. Other symptoms of toxic response to a chemical include fever, hair loss, headache, nausea, rash, urine abnormalities, and numbness in arms and legs. Regardless of the response that is used for measurement with respect to dose, toxicologists find that the form of the dose-response curve is similar.

Notes About Lesson 3

In this lesson, students will use the data they collected on the germination of their seeds in the presence of a chemical to create a dose-response curve for their chemical. In doing so, students visually will be able to compare the slope of their chemical's curve with those of other students. Students also can compare the potency of the chemicals by measuring germination of seeds. It is important for students to remember that they cannot make inferences about the potency of the chemicals with respect to human health, but they can only use their data to inform them of the chemicals' potential toxicity to humans. In this way, students must think critically and logically to make the relationships between evidence and explanations.

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	yes (optional)
Extension Activity	no

Photocopies		
Activity Number	**Master Number**	**Number of Copies**
Activity 1	Master 3.1, *Dose-Response Curves* Master 3.2, *Graph Paper*	1 transparency 1 for each student
Extension Activity	none	none

Materials	
Activity 1	**Extension Activity**
For the class: • overhead projector • transparency of Master 3.1, *Dose-Response Curves* • blank transparency • overhead markers **For each team of 3 students:** • bags of seeds treated with chemical from Lesson 2 (print version) **For each student:** • Master 2.3, *Toxicity Testing on Seeds*, from Lesson 2 • data from the CD-ROM (optional) • 1 copy of Master 3.2, *Graph Paper* • pencil	**For each team of 3 students:** • materials for laboratory investigation from Lesson 2, Activity 2.

PREPARATION

Activity 1

If your students conducted the CD-ROM version of Lesson 2, arrange for students to have access to computers.

Make a transparency of Master 3.1, *Dose-Response Curves*.

Duplicate Master 3.2, *Graph Paper*, 1 for each student.

Extension Activity

Gather the materials needed for students to conduct their investigation.

Procedure

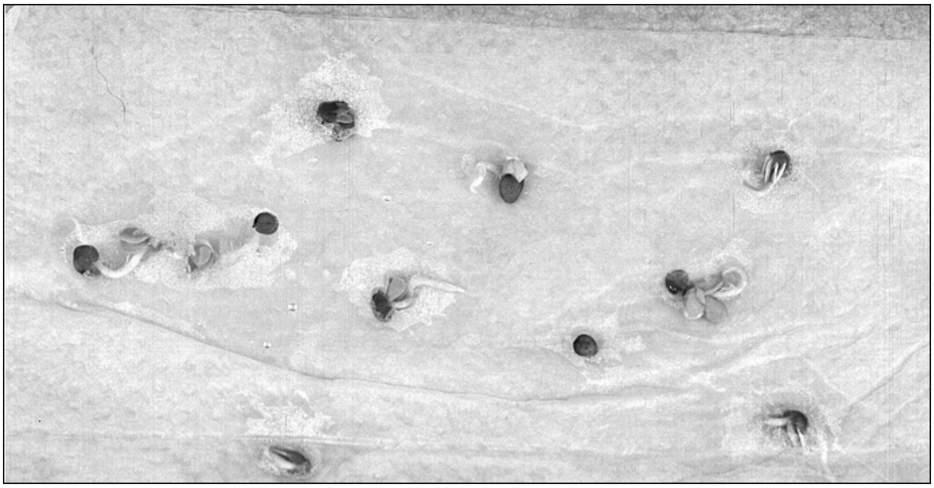
ACTIVITY 1: GRAPHING THE RESPONSE TO CHEMICAL DOSE

If students are investigating seed germination using the CD-ROM, direct students to access the data on the CD-ROM and proceed to Step 3 of this activity (see Lesson 2, Activity 4).

1. **As the students enter the room, ask them to get their bags of seeds treated with chemicals from Lesson 2 and bring them to their team's table.**

2. **Direct students to observe each of their six bags of seeds. Ask them to record in the Day 3 column of their data table the number of seeds in each population that have germinated and the number of seeds that have not germinated.**

   Students might see more than just germination: Some plants now might be developing leaves. Encourage students to note any growth in the margin of their data table.



Content Standard A: Students use appropriate tools and techniques to gather, analyze, and interpret data.

3. **Once students have completed their data table, tell them that scientists graph data like theirs to help them understand the relationship between dose and response and make judgments about the safety of particular chemicals. Be sure to point out that students can assume that the dose the seeds receive is related to the concentration of the chemicals in each bag. Display the sample graphs of dose-response relationships on the transparency of Master 3.1, *Dose-Response Curves*.**

Point out to students that, in the top graph, the dose of alcohol is along the *x*-axis and the response is graded along the *y*-axis, from no effect to death. On the second graph, the dose of chemical in milligrams is along the *x*-axis. The response, the incidence of tumors in a population of mice, is along the *y*-axis. Use the *Background Information* to provide information for students about the two types of dose-response curves, for individuals and for a collection of subjects.

It might be of interest to your students to think about a word that often describes a person who has had too much to drink: *intoxicated*. Using their knowledge of toxicology, students should recognize that the base of the word, *toxic*, accurately describes what happens when a person is drinking. A person who is drinking alcohol is exposing himself or herself to a toxic substance that, at a high enough dose, can cause death. Impress upon students that the dose-response curve on the overhead provides evidence that binge drinking (which provides a high dose of alcohol in a very short time) can be very dangerous, and even deadly.

Content Standard A: Students use mathematics in all aspects of scientific inquiry.

4. **Tell students that you would like them to graph the data they recorded for Day 3 of their seed investigation. Using a blank transparency, work with students to design a graph that shows the relationship between dose and response. To do that, students will need to help you decide the following:**

- **Which of the two types of dose-response graphs will they use?**

Students will want to use the dose-response graph that represents data from a population of individuals.

- **What is the response that you want to graph?**

This is sometimes counterintuitive for students. The response that they want to graph is the one caused by the chemical (the response that was different from the response of the control group). In most cases, the response is the lack of germination, so students would graph the number of seeds in the population that did *not* germinate.

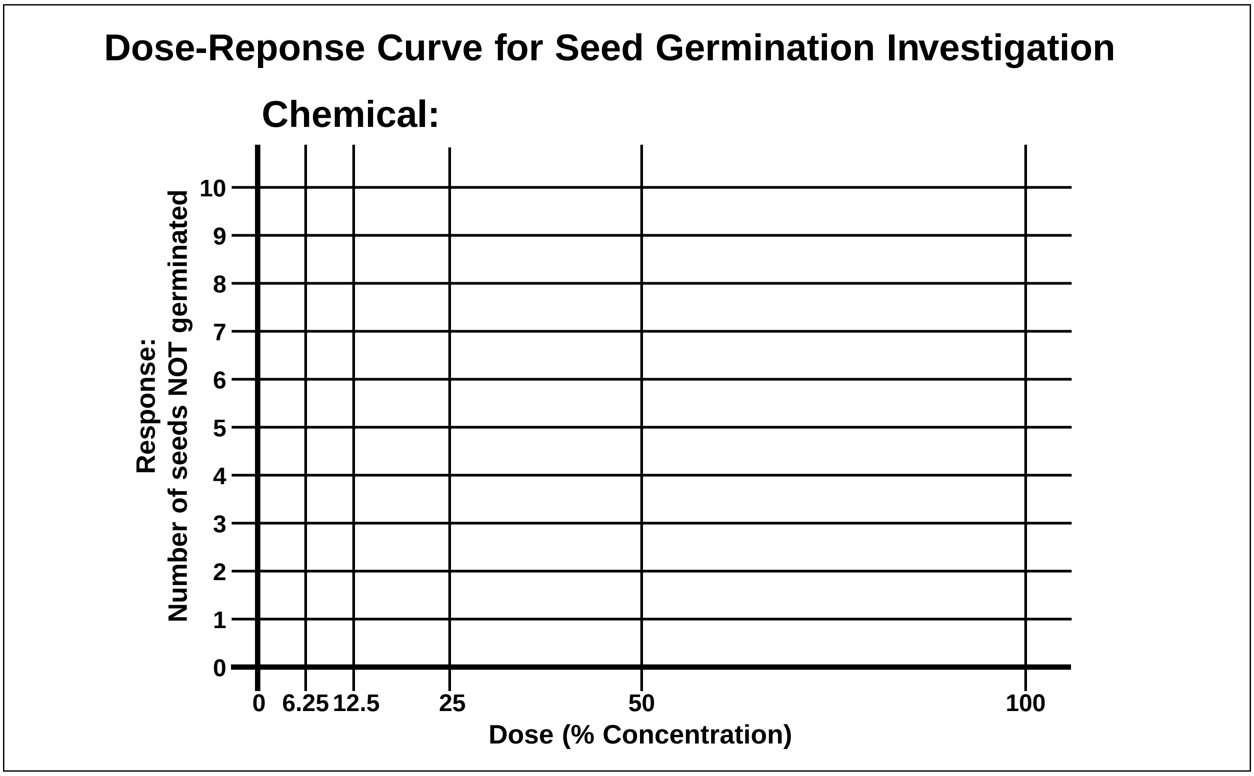
- **What measurement should be on the *x*-axis?**

The dose is recorded along the *x*-axis, in increasing concentrations from 0% to 100%. Help students recognize that they need to space their measurements accurately along the *x*-axis, but not at even intervals since their concentrations are 0%, 6.25%, 12.5%, 25%, 50%, and 100%.

- **What measurement should be on the *y*-axis?**

The response is recorded along the *y*-axis, as the number of seeds in the population that did not germinate, from 0 to 10.

When you are finished making a sample of the graph, it should look like the following graph:

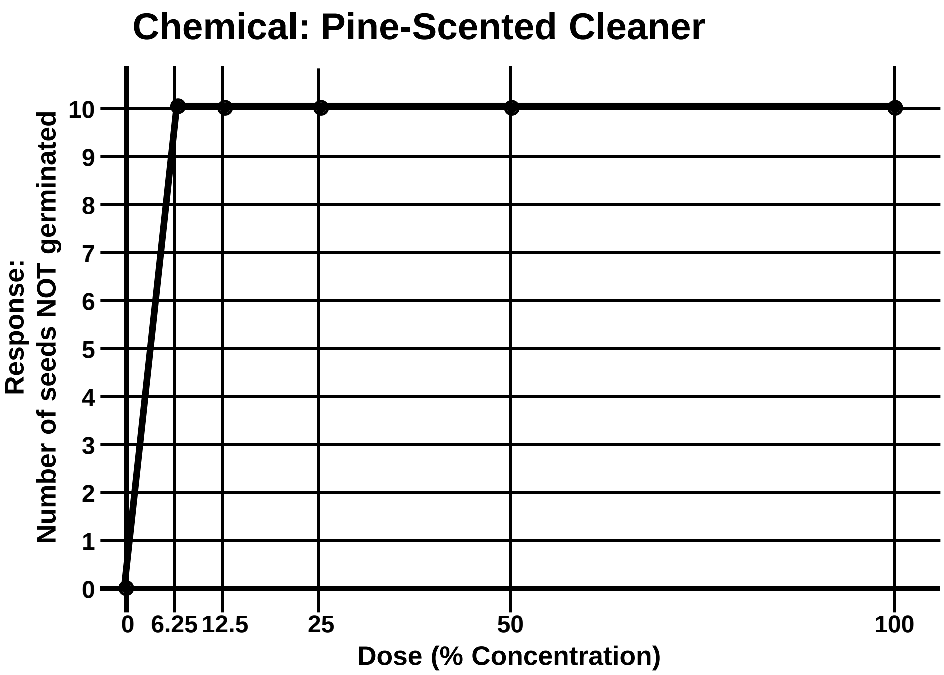


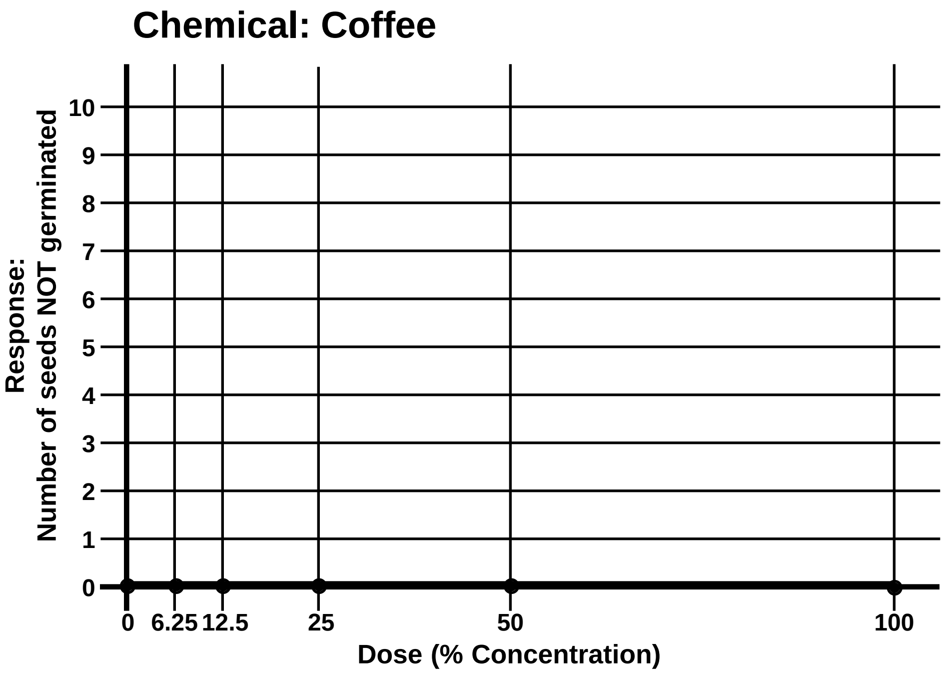
5. **Distribute copies of Master 3.2, *Graph Paper*, one to each team. Direct teams to make a dose-response graph for their chemical on Graph A.**

Remind students to label their graph with the name of their chemical.

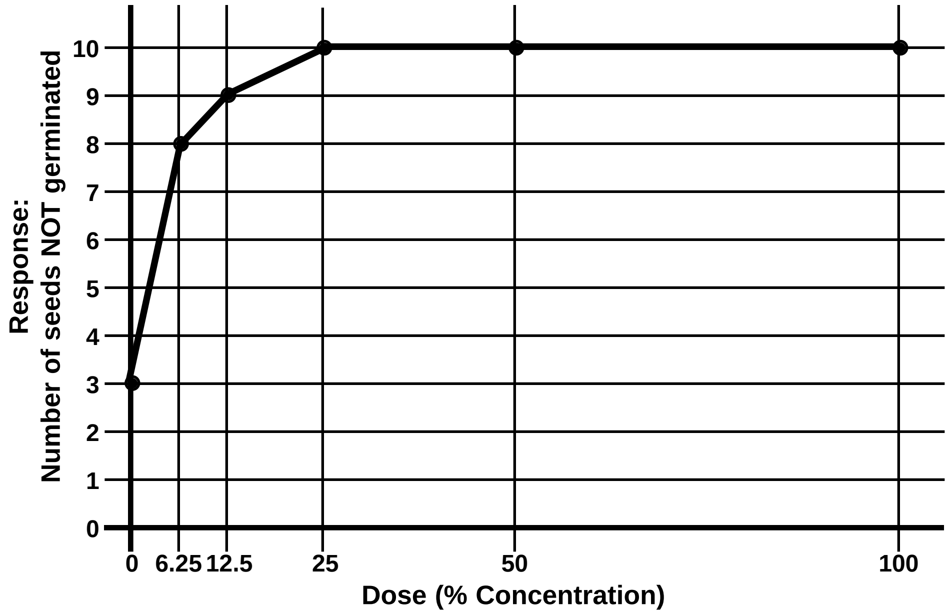
6. **Once teams have made a graph of their chemical, instruct them to get data from two other teams that tested different chemicals. Tell teams to graph the data on Graphs B and C, remembering to label each graph with the name of the chemical.**

Tip from the field test: Included here are several dose-response graphs for chemicals tested by students who participated in the field test.

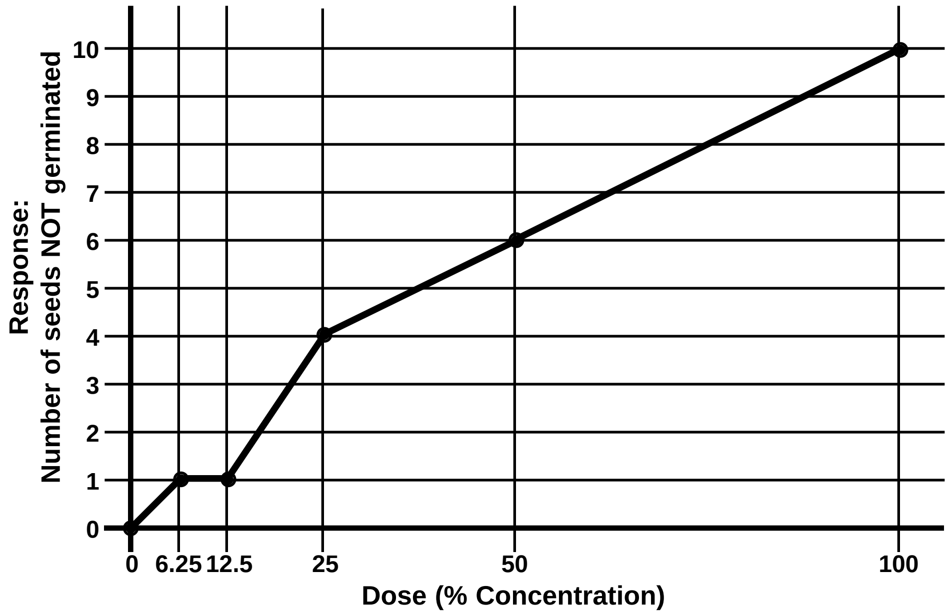


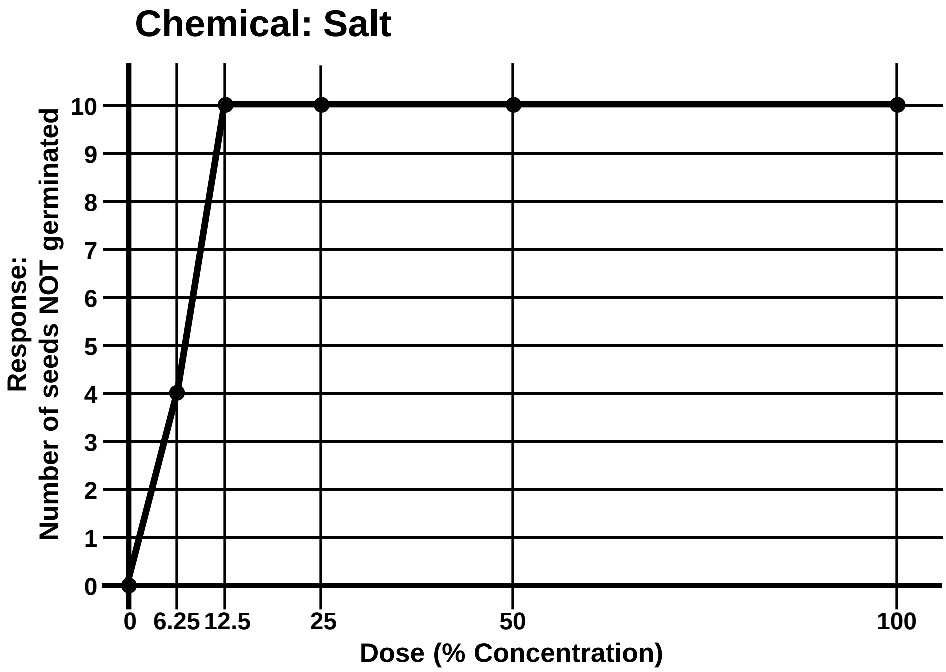


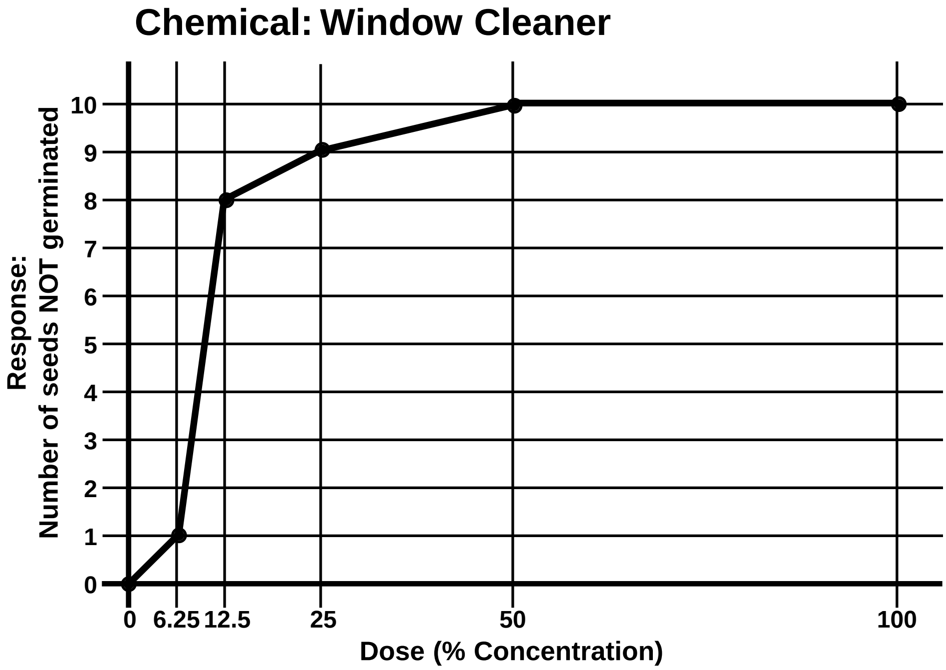
Chemical: Insect Repellent



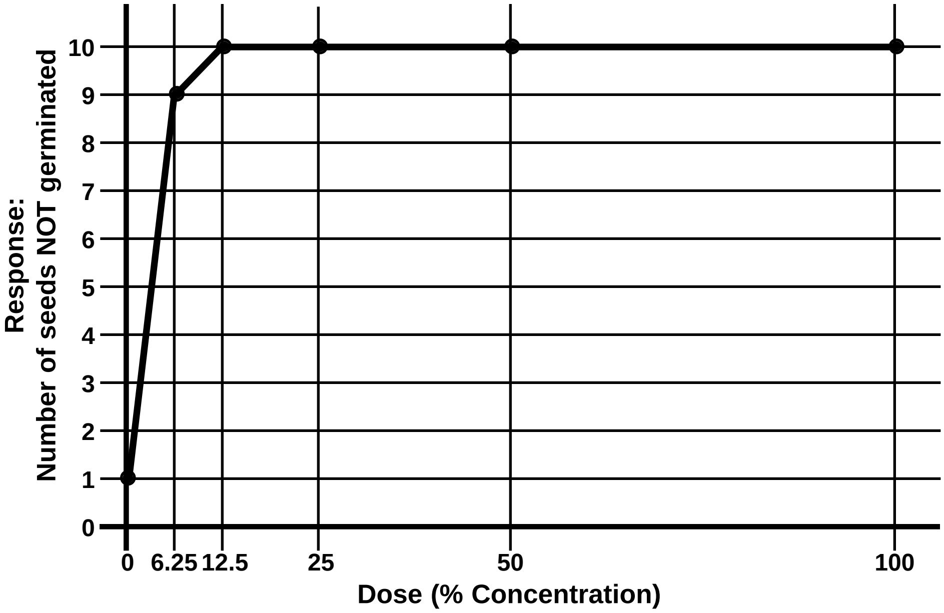
Chemical: Fruit Punch Soda




Chemical: Salt
Response:
Number of seeds NOT germinated
0
1
2
3
4
5
6
7
8
9
10
0
6.25
12.5
25
50
100
Dose (% Concentration)


Chemical: Window Cleaner
Response:
Number of seeds NOT germinated
0
1
2
3
4
5
6
7
8
9
10
0
6.25
12.5
25
50
100
Dose (% Concentration)

Chemical: Water-Soluble Plant Fertilizer



7. Circulate around the room and, as they work, ask the teams to study the team graphs to decide which chemical had the highest potency or which chemicals have a clear threshold.

Of the chemicals graphed above, Lysol (pine-scented cleaner) is the most potent and coffee is the least potent. Field-test students found that it was difficult to determine threshold. They knew only that they exceeded the threshold below which there was no effect when they used Lysol, salt, window cleaner, bug repellent, fruit punch soft drink, and plant fertilizer. To pinpoint the exact threshold, students would need to repeat their investigation using additional concentrations between 0% and 6.25%. When they tested coffee, students found no threshold: Coffee had no effect on seed germination even at 100% concentration.

Listen to students' descriptions of the dose-response curves to see if they understand the concepts of threshold and potency.

8. Discuss with students what conclusions they can make, if any, about the safety or potential harm of the chemicals tested for humans. Ask students to evaluate the use of plants as a model system for toxicology testing.

Students should recognize that plants do not have the same structure as humans or other animals, so results from tests that determine toxicity to plants may not apply to humans. In fact, there are chemicals that are toxic to plants that do not harm humans and, conversely, there are chemicals that do not harm plants but are capable of harming animals like humans. For this reason, it is best to test chemicals on systems that most closely resemble the human system if knowledge about effects on humans is the goal. Even so, students may recognize that data from toxicity tests on seeds could help inform them of possible toxicants to humans.

Content Standard A: Students develop descriptions, explanations, predictions, and models using evidence.

Content Standard A: Students think critically and logically to make the relationships between evidence and explanations.

Toxicologists use to their advantage their understanding that it is possible for some chemicals to cause injury to one kind of living matter without harming another kind of living matter. By understanding this biological phenomenon, scientists can, for example, help farmers develop pesticides that are lethal to fungi or insects but do not harm crops, or antibiotics that kill infectious bacteria (also living organisms) but have low toxicity in humans.

Extension Activity

Ask students to describe other questions they would like to answer about the effects of their chemical on plants. Allow space and time for students to investigate their questions.

For example, students might want to know if their chemical has an effect on the growth of plants. They can sprout seeds and then water the seedlings with varying concentrations of chemical solutions. By setting up an investigation that can last a longer time, students can experiment with the concept of exposure over time. They can administer a small dose of chemical repeatedly for many days and compare the responses to those in plants that receive only one large dose of chemical.